CASE REPORT

Acetaminophen Toxicosis in a Cat

J. O. ANVIK

Sardis Animal Hospital, Box 128,
Sardis, British Columbia V2R 1A5

Summary

A seven month old domestic shorthaired male cat was presented with a known history of acetaminophen ingestion. Clinical findings included icterus, depression, hypothermia, tachypnea and pronounced edema of the head and neck. Treatment was aimed at providing substrate to assist in conjugation of the drug and reversing methemoglobinemia. Administration of oral acetylcysteine, ascorbic acid and IV fluids was insufficient in this case due to a delay in initiation of treatment. The salient postmortem findings were icterus, subcutaneous and pulmonary edema and evidence of hemolysis in the liver, spleen and urinary tract.

The pathophysiology of the toxicosis and the current recommendations for treatment are reviewed.

Key words: Acetaminophen, toxicosis, cat, poison, icterus, acetylcysteine.

Résumé

Empoisonnement d'un chat par l'acétaminophène

Cet article porte sur un chat domestique, âgé de sept mois, et amené à une clinique vétérinaire par son propriétaire, parce qu'il avait ingéré de l'acétaminophène. Il manifestait les signes cliniques suivants: ictère, dépression, hypothermie, tachypnée et oedème marqué de la tête et du cou. Le traitement visait à fournir un substrat destiné à favoriser la conjugaison de la drogue et à arrêter la formation de méthémoglobine. L'administration buccale d'acétylcystéine et d'acide ascorbique, ainsi que l'injection intraveineuse d'électrolytes, se révélèrent insuffisantes, parce que trop tardives. La nécropsie du chat démontra les lésions proéminentes suivantes: ictère, oedème sous-cutané et pulmonaire, ainsi que l'évidence d'une hémolyse, dans le foie, la rate et les voies urinaires.

L'auteur présente la pathophysiologie de cet empoisonnement et les recommandations courantes, relatives à son traitement.

Mots clés: acétaminophène, toxicose, chat, poison, ictère, acétylcystéine.

Introduction

The common use of acetaminophen by people leads some cat owners to assume the drug is safe for cats. Veterinarians occasionally are presented with acetaminophen toxicosis in cats but the total number of cases is not known. One report reviewing the files at the Animal Poison Control Center, University of Illinois, Urbana, Illinois cited 89 cases during a two year period (1).

Cats are reported to be deficient in the specific glucuronyl transferase enzyme required for the conjugation of exogenous aromatic ring compounds such as acetaminophen (1). This results in much slower conjugation rates than other species (1,2). The net effect is the accumulation of toxic reactive metabolites which bind covalently to macromolecules leading to death of liver cells and other tissues. Reactive metabolites also oxidize hemoglobin to methemoglobin, resulting in diminished oxygen transport and tissue anoxia.

In the presence of adequate hepatic glutathione, toxic metabolites will preferentially conjugate with glutathione, producing nontoxic mercapturic acid conjugates, thereby sparing hepatocytes from molecular damage. Cell death can result when liver glutathione stores become depleted. Studies in the cat have also shown that erythrocyte glutathione levels are depleted in acetaminophen toxicosis (4). Erythrocyte glutathione acts as a reserve antioxidant to assist the methemoglobin reductase enzymes when they are overwhelmed by high rates of methemoglobin production. Erythrocyte glutathione depletion thereby diminishes the protective antioxidant effect and results in abnormally high levels of methemoglobin. Since cats have more reactive sulfhydryl groups on the hemoglobin molecule (eight as opposed to four in the dog and two in man), it is more difficult to keep hemoglobin reduced under conditions of oxidant stress (3). This may partially explain the increased species susceptibility to methemoglobin production in the cat.

The excessive accumulation of methemoglobin is the most significant physiological abberation in acetaminophen toxicosis in cats. It leads to denaturation of hemoglobin, Heinz body formation, increased osmotic fragility of red blood cells and hemolytic anemia. Icterus, hemoglobinemia, hemoglobinuria, tissue anoxia and cyanosis then appear.

The rationale for the treatment of acetaminophen intoxication with acetylcysteine is based on its ability to provide the cysteine moiety required for increased synthesis of glutathione (1). It also provides suitable substrate to enhance conjugation and elimination of the drug. Adjunctive therapy with ascorbic acid is reported to be of benefit (1). Its primary action is to reduce the methemoglobin already formed. In addition, ascorbic acid may also supplement the endogenous protective ability of reduced glutathione in minimizing covalent binding of toxic metabolites and their subsequent cellular toxic effects.

The purpose of this report is to describe clinical and postmortem findings in a cat known to have ingested acetaminophen and to review the current recommendations for therapy.

History

A 3.25 kg seven month old male domestic short-haired cat was admitted three days after having been castrated without anesthesia by a non-veterinarian. In an attempt to relieve the postoperative discomfort, 250 mg of acetaminophen (Tylenol, McNeil Laboratories (Canada) Ltd., Stouffville, Ontario) was administered to the cat by the owner and a second 250 mg was given twelve hours later. According to the owner, the cat's nose, lips and paws turned grey shortly after the second dose. About ten hours later the face became swollen and the cat became restless. The owner reported jaundice and depression 48 hours after the initial therapy and presented the cat in a state of collapse 72 hours after initial treatment.

Clinical Findings

Depression, slight dehydration, mild abdominal discomfort and edema of the face, lips, submandibular skin and ventral neck were readily apparent. The mucous membranes, sclera and skin were profoundly icteric. Further examination revealed a rectal temperature of 36.9°C, harsh lung sounds, rapid shallow respirations and a rapid feeble pulse. Blood for serum chemistry was drawn and the results are tabulated in Table I.

TABLE I
SERUM CHEMISTRY PROFILE OF A CAT WITH ACETAMINOPHEN POISONING

Glucose	220 mg/dL	(70-125)[a]
BUN	45 mg/dL	(10-35)
Creatinine	0.0 mg/dL	(1-2)
Sodium	140 mEq/L	(145-155)
Potassium	4.0 mEq/L	(4.0-5.8)
Calcium	9.0 mg/dL	(6.0-10.0)
Phosphorus	11.3 mg/dL	(5.2-7.0)
Total protein	7.4 g/dL	(1.0-8.0)
Albumin	3.2 g/dL	(2.6-4.0)
Globulin	4.2 g/dL	(2.6-5.1)
Total bilirubin	7.6 mg/dL	(0.0-0.1)
Direct bilirubin	4.5 mg/dL	(0.0-0.2)
Alk PO4	0.0 IU/L	(10-70)
SALT	302 IU/L	(5-62)

[a] Normal values in brackets.

Treatment

Upon presentation the cat was treated with acetylcysteine (Airbron, Allen & Hanburys, Glaxo Canada Ltd., Toronto) at a dose of 140 mg/kg diluted to a 5% solution in water and given orally. Vitamin C (Vitamin C tablets B.P., Novopharm Ltd., Toronto) 250 mg was given orally and dextrose 5% in water was given intravenously. In spite of therapy the cat died two hours after being admitted and the entire carcass was submitted for necropsy.

Pathology Findings

The carcass was in good condition but there was moderate icterus and edema of the face and neck. Some blood was present at the castration site.

There was marked subcutaneous edema in the ventral cervical and intermandibular areas and bright yellow pigmentation of body fat. Excessive serosanguinous fluid filled the thoracic cavity and pericardial sac. Mediastinal edema was also prominent. The trachea and mainstem bronchi were froth-filled and extensive fluid suffused from the cut surface of the lung. The kidneys were dark and the urinary bladder contained 3 mL of very dark red urine. The liver was slightly enlarged and icteric and the gall bladder was distended. Moderate splenic congestion was also noted.

Microscopic examination of the CNS, eye, adrenal gland, stomach, jejunum and bone marrow revealed no significant alterations. Specific hepatocellular changes were not observed but there was moderate biliary stasis and Kupffer cell erythrophagocytosis. There was hyperplasia of the monocyte-phagocytic system of the spleen and erythrophagocytosis. The renal glomeruli, convoluted tubules and urinary bladder contained erythrocytic debris. Light-staining proteinaceous fluid flooded the pulmonary alveoli and there were increased numbers of alveolar macrophages, many containing hemosiderin. Mild edema and hemorrhage separated some degenerate cardiac myofibres. Focal areas of myocarditis with neutrophilic infiltrates occurred occasionally within these affected areas.

Discussion

It would appear that acetaminophen produced clinical findings and pathology in this cat similar to those described elsewhere (2,4,5). The pathogenesis of the edema, presumably, is methemoglobin-induced anoxia leading to increased permeability of capillary walls.

The concurrent myocarditis and mild cardiomyopathy presumably contributed to the cat's demise. Whether the cardiac lesions were due to preexisting disease or from sepsis introduced by improper castration is unknown. It is improbable that the myocarditis was drug-induced as it has not been previously reported and is inconsistent with the known pathophysiology of acetaminophen toxicosis.

Light microscopic lesions were not noted in hepatocytes in spite of elevated serum alanine aminotransferase (SALT) values. Acute toxicosis does not cause visible hepatic lesions (4,6). However, one study of cats given acetaminophen over a longer term demonstrated liver necrosis (4).

Hyperbilirubinemia and increased SALT were the most significant abnormalities in serum chemistry. The hyperglycemia is probably stress-related and it is assumed that hemolysis accounts for the elevated phosphorus level. Hemolysis interfered with the creatinine reading.

The current recommended treatment protocol for acute acetaminophen toxicosis in the cat is as follows (1):

1) If recent (less than two hours) ingestion has occurred, induce vomition and treat with activated charcoal at a dose of 2 g/kg body weight along with a saline cathartic such as sodium sulfate (0.5 g/kg body weight) as a 20% slurry.
2) Acetylcysteine supplied commercially as a 20% solution (Airbron or Mucomyst, Bristol Laboratories of Canada, Ottawa) is given orally at a dose of 140 mg/kg. This dosage may be reduced to 70 mg/kg and repeated at six hour intervals for 36 hours or until clinical improvement is noted.
3) Vitamin C (ascorbic acid) at a dose of 30 mg/kg orally or parenterally repeated at the same interval as above.

4) Supportive care including oxygen, IV Lactated Ringers solution, furosemide and injectable B vitamins.

Antihistamines are contraindicated as they increase the toxicity of acetaminophen (2,6). Steroids are not recommended (1).

Toxicity studies suggest that acetaminophen ingestion as high as 140 mg/kg can be treated successfully if therapy is initiated within four to six hours of ingestion. The total dose given to this cat was approximately 150 mg/kg. The long delay in presenting the cat for treatment presumably accounts for the fatal result.

The biochemical idiosyncrases of the cat can lead to devastating consequences when drugs that are poorly metabolized are administered. The cat's inability to conjugate and eliminate the drug effectively, combined with owners lack of appreciation of the dose-body weight difference between humans and cats can easily explain the poisoning. Acetaminophen is not recommended at any dose in the cat (2).

Acknowledgments

The author is grateful to Dr. Ron Lewis for assistance with the interpretation of the pathology and the preparation of the manuscript.

References

1. CULLISON RF. Acetaminophen toxicosis in small animals: Clinical signs, mode of action and treatment. Compend Cont Educ 1984; 16: 315-321.
2. BOOTH NH. Nonnarcotic analgesics. In: Booth NH, McDonald LE, eds. Veterinary pharmacology and therapeutics, 5th ed. Ames, Iowa: Iowa State University Press, 1982: 301-305.
3. NASH SL, OEHME FW. A review of acetaminophen's effect on methemoglobin, glutathione and some related enzymes. Vet Hum Toxicol 1984; 26: 123-132.
4. GAUNT SD, BAKER DC, GREEN RA. Clinicopathologic evaluation on acetylcysteine therapy in acetaminophen toxicosis in the cat. Am J Vet Res 1981; 42: 1982-1984.
5. FINCO DR, DUNCAN JR, SCHOLL WD, PRASSE DW. Acetaminophen toxicosis in the cat. J Am Vet Med Assoc 1975; 166: 469-472.
6. ST OMER VV, McKNIGHT ED. Acetylcysteine for treatment of acetaminophen toxicosis in the cat. J Am Vet Med Assoc 1980; 176: 911-913.